Amendments to the Specification:

Please replace the paragraph bridging pages 12 and 13 of the application as filed with the following amended paragraph:

In another aspect, the present invention provides a synthetic oligonucleotide complementary to at least two non-contiguous regions of an HCV messenger or genomic RNA. Non-contiguous oligonucleotides are targeted to at least two regions of the HCV genomic RNA or mRNA which are not contiguous in a linear sense but, which may be next to each other in three dimensional space due to the secondary structure or conformation of the target molecule (FIGS. 2A and 2B). In preferred embodiments, one or both portions of the ~~non-contiguous"~~ non-contiguous oligonucleotide is complementary to the 5' untranslated region. One portion of some non-contiguous oligonucleotides includes the same 12 bases (bases 100-111) designated the "anchor" region. The other portion of such ~~noncontiguous~~ non-contiguous oligonucleotides is variable, containing 6 to 12 bases within, e.g., bases 315-340 of HCV nucleic acid. In one embodiment, one portion which is complementary to the 5' untranslated region comprises the sequence GGGGUCCUGGAG (SEQ ID NO:47), and the other portion is complementary to a 5' region of the RNA encoding the HCV C protein. Other non-contiguous oligonucleotides of the invention may be targeted to other non-contiguous regions of HCV nucleic acid. For example, in another embodiment, the portion which is complementary to the 5' untranslated region and which functions as an anchor comprises the sequence CAACACUACUCG (bases 243-254). In preferred embodiments, the non-contiguous oligonucleotide [[has]] is about 18 to about 24 nucleotides in length.

Please replace the paragraph at page 15, lines 1-19, with the following amended paragraph:

In this aspect of the invention, a therapeutic amount of a pharmaceutical composition containing HCV-specific synthetic oligonucleotides is administered to the cell for inhibiting hepatitis C virus replication or of treating hepatitis C virus infection. The ~~HCVspecific~~ HCV-specific oligonucleotides are the contiguous or non-contiguous oligonucleotides of the

invention. In some preferred embodiments, the method includes administering at least one oligonucleotide, or at least two contiguous oligonucleotides, having a sequence set forth in Table lF or in the Sequence Listing as SEQ ID [[NO:2,]] NO: 2, 5, 6, 7, 8, 14, 15, 16, 17, 23, 24, 26, 27, 28, 29, 31, 33, 34, 36, 37, 47, 68, 69, 70, 71, 72, 73, 74, 75, 76, and 77 or as set forth in Tables 1A and 1B as SEQ ID NOS: 78-133, or a combination thereof. In other preferred embodiments, the method includes administering at least one noncontiguous oligonucleotide, or at least two non-contiguous oligonucleotides, having a sequence set forth in Table 2 or in the Sequence Listing as SEQ ID NO: 38, 39, 40, 41, 42, 43, 44, 45, 46, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, and 67, or as set forth in Tables lC-lE as SEQ ID NOS: 134-172, or a combination thereof. The oligonucleotides may also be used in modified form.

Please replace the paragraph bridging pages 15 and 16, with the following amended paragraph:

In another aspect, the invention provides a method of detecting the presence of HCV in a sample, such as a solution or biological sample. In this method, the sample is contacted with a synthetic oligonucleotide of the invention. Hybridization of the oligonucleotide to the HCV nucleic acid is then detected if the [[HPV]] HCV is present in the sample.

Please replace the paragraph at page 19, lines 4-14, with the following amended paragraph:

Another form of a hybrid is an "inverted" hybrid oligonucleotide which includes an oligonucleotide comprising a 2'-O-substituted (or 2' OH, unsubstituted) RNA region which is interposed between two oligodeoxyribonucleotides regions, a structure that is inverted relative to the "traditional" hyrbid oligonucleotides. Hybrid and inverted hybrid oligonucleotides may be ~~syntesized~~ synthesized as described in the Examples for oligonucleotides containing 2'-O-methyl RNA. The hybrid and inverted hybrid oligonucletides of the invention are particularly preferred due to the enhanced stability and activity over time in the presence of serum. In

another embodiment the hybrid or inverted hybrid may comprise at least one n-butyl phosphoramidate or methylphosphonate linkage.

On pages 29 and 30, please replace all occurrences of "triples-forming" with "triplex-forming"in the column entitled "Description" of TABLE 1E.

Please replace the paragraph at page 43, lines 11-21, with the following amended paragraph

Treatment of HepG2 HCV (52-1417) cells with antisense oligonucleotide decreased the amount of HCV specific RNA, as shown in FIGS. 11A and 11B. HepG2 cells which were not transfected with the HCV construct do not produce a specific, HCV related band with probe 1 (FIG. 1 1A). Similar experiments were conducted to show the specificity of probe 2 (FIG. 11B). FIG. 11A and 11B show that [[HCVt]] HCV1 and HCV3 decreased HCV RNA in HCV (52-1417) cells. The amounts of full length HCV RNA were quantitated on the phosphorimager and compared to untreated cells (Table 3).

Please replace the paragraph bridging pages 66 and 67, with the following amended paragraph:

HepG2 cells ([[ATCC]] ATCC® MB8065, American Type Culture Collection, ~~Rockville, MD~~ Manassas, VA) were maintained in DMEM with 10% fetal calf serum. Cells were transfected with pcHCV LUCneo by the calcium phosphate procedure (Sambrook et al. (1989) *Molecular Cloning, A Laboratory Manua*l (2nd ed.), Cold Spring Marbor Laboratory Press, pp. 16.30-16.40). Stably transfected clones were selected with (0.75 μg/ml) Geneticin (Gibco/BRL, Gaithersburg, MD). Clones were evaluated for luciferase expression as described below. A similar luciferase construct lacking HCV sequence was also expressed stably in HepG2 cells.

Please replace the paragraph at page 70, lines 4-21, with the following amended paragraph

HCV bases 1-2545 were used to generate a recombinant virus with Semliki Forest virus (SFV/HCV) (Gibco/BRL, Gaithersburg, MD). HCV sequences were subcloned from vvl-2545 (Hoffmann-La Roche, Basel, Switzerland) into pSFVl. SFV/HCV sequences were transcribed in vitro using SP6 RNA polymerase. RNA was also transcribed from pSFV2-Helper (Gibco/BRL, Gaithersburg, MD) which provided SFV structural proteins to the recombinant virus. The two RNAs were co-transfected into BMK2l cells (~~ATCC Ac.~~ ATCC® No. CCL 10, American Type Culture Collection, ~~Rockyille, MD~~ Manassas, VA), according to the manufacturer's instructions (SFV Gene Expression System, Gibco/BRL, Gaithersburg, MD.) to generate the recombinant virus. Supernatant was removed from the cultures 48 hours post-transfection and used as a virus stock for subsequent experiments. pSFV2-Helper produces a structural protein (p62) containing an eight base mutation, converting three arginines to non-basic amino acids. This modification renders the recombinant virus non-infectious unless the p62 protein is first digested with chymotrypsin (Gibco/B RL, Gaithersburg, MD). Recombinant virus required chymotrypsin activation before infection.